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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,194	09/23/2004	Ramon Alemany Bonastre	16596-049US1	7846
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			EXAMINER PRIEBE, SCOTT DAVID	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 06/07/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/509,194

Applicant(s)

BONASTRE ET AL.

Examiner

Scott D. Priebe, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 March 2007 and 10 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,5-10,13,15-17 and 19 is/are allowed.
- 6) ☒ Claim(s) 3,4,11 and 18 is/are rejected.
- 7) ☒ Claim(s) 12 and 14 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>20070321</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The amendment filed 10/22/2003 during examination of PCT/ES03/00140 remains objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows.

In the 10/22/03 amendment, page 10a includes a new paragraph for which there was no counterpart in original pages 8-10, where the adenovirus is dl331. This subject matter is present in the amendment filed 5/10/07 in page 5, lines 15-17. This prior art adenovirus does not, as implied by the first two paragraphs of page 8a (first two paragraphs of the amendment text on page 2 of 5/10/07 amendment) have defective VAI and VAII genes. It is an hAd5 strain with has a defective VAI gene, due to the dl331 mutation, but not a defective VAII gene, i.e. a functional wild type VAII gene is present.

Applicant is required to cancel the new matter in the reply to this Office Action. Applicant provides no argument to this part of the original rejection, but essentially the same issue is argued with respect to the rejection of claim 11 for new matter, which are addressed below.

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Claim Objections

Claim 14 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 5.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 12 and 14 are objected to because of the following informalities. A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n). Claims 12 and 14 depend from dependent claims, but are separated therefrom by dependent claims that do not depend from the same dependent claims. Appropriate correction is required prior to allowance, and may be effected by Examiner's amendment at allowance.

Claim Rejections - 35 USC § 112

Claims 3 and 11 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record set forth in the Office action of 12/21/06. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Applicant's arguments filed 5/10/07 have been fully considered but they are not persuasive. With respect to claim 11, Applicant indicates that this claim was supported by Examples 1-3, which describe using dl331, and the teachings on page 7, lines 4-7, and pages 8a-10. First, pages 8a, 9a, and 10a are not part of the original disclosure, and cannot be relied upon for providing support for the embodiment of using a strain derived from dl331 in which the VAI gene has also been mutated. It remains that there is no suggestion in the original disclosure of an embodiment of the method where adenovirus used is derived from dl331 by mutating the VAI gene. "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997).

With respect to claim 3, Applicant asserts that a "number of genes that control expression of the VAI or VAI genes were known in the art at the time of filing, and one of skill in the art would readily be able to identify and select these genes," but provides no evidence to support this assertion. "Argument of counsel cannot take the place of evidence lacking in the record." *In re Scarbrough*, 182 USPQ 298, 302 (CCPA 1974). The only adenoviral gene disclosed in the specification as controlling expression of the VAI and VAI genes is E1A. The specification provides no guidance as to any other adenoviral genes that have the required function, or evidence that any such other adenoviral genes were well known to those of skill in this art.

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Claim 4 remains rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 12/21/06, because the specification, while being enabling for treating "cancer" resulting from human tumor cells by administering an adenovirus that selectively replicates in the human cancer cells, wherein the adenovirus is descendent from a human adenovirus having a VAI gene and a VAII gene by mutation of the VAI and VAII genes such that the genes are inactivated and the human tumor cells have a constitutively active Ras pathway or are unresponsive to exposure to interferons, and wherein the adenovirus may additionally have mutations in E1a or E1b genes that result in further selective replication in tumor cells or have promoters operably linked to E1a, E1b or E4 that result in further selective replication in tumor cells, does not reasonably provide enablement for any other embodiments readable on the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed 5/10/07 have been fully considered but they are not persuasive. Applicant asserts that "in the parlance of a person of skill in the art, a "gene" is generally considered to include a coding or transcribed region, as well as any regulatory elements including promoters and repressors," but provides no evidence to support this assertion. "Argument of counsel cannot take the place of evidence lacking in the record." *In re Scarbrough*, 182 USPQ 298, 302 (CCPA 1974). In the adenoviral art, one commonly refers to "regions" rather than genes, e.g. the E4 region. The E4 region has 7 different open reading frames (E4 ORF1 through E4 ORF7), and the specification does not provide guidance identifying any mutations in any of these open reading frames that will confer tumor-selective

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replication. While the specification does teach that the E4 promoter can be modified to confer tumor-selective replication, this teaching is not commensurate in scope to that of the claim, which does not limit the mutation to the E4 promoter, i.e. it embraces mutations in the open reading frames that would provide the required function.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recited limitations of claim 18 do not make sense. In line 1, the claim refers "said mutated VAI and VAII genes", i.e. the mutations are within the genes. However, lines 3-4 indicate that the mutations are "in a sequence before a VAI or VAII gene" and "in a sequence after a VAI or VAII gene", i.e. outside the genes. The mutations cannot be both within and outside of the genes. As a result, it is unclear what sequences that control the expression or termination of the VAI or VAII gene are being referred to here.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

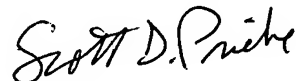
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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Scott D. Priebe, Ph.D.
Primary Examiner
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